ORIGINAL REPORT

A Novel Protocol for Gastric Lavage in Patients with Aluminum Phosphide Poisoning: A Double-Blind Study

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Abstract- Aluminum phosphide poisoning (ALPP) still has no efficient and approved antidote. Supportive care and hemodynamic monitoring are the only choices of treatment. We proposed a new lavage formulation in addition to evaluation of its efficacy and defining the impact of clinical characteristics of patients on their prognosis. During eight months period of time, 120 patients were enrolled to the study and randomly received two different gastric lavage protocols. Our new lavage protocol had positive impact on patients' survival and the *P*-value in comparison with the classic gastric lavage method was close to significant level (*P*=0.054). On hospital arrival indication for intubation-ventilation as well as sense of thirst, sore throat and absence of nausea indicate worse outcome. Using our novel approach, indication for intubation-ventilation as well as sense of thirst, sore throat and absence of nausea can be considered as applicable prognostic factors in survival of ALPP patients. Further studies are required to set this approach as preferred treatment.

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Introduction

Aluminum phosphide poisoning (ALPP) is common in Asia, especially in India, Jordan, Morocco and Iran due to its frequent use as a fumigant in grain storage facilities. In parallel with its accidental ingestion, it has been used frequently as a suicidal agent as well (1-5). Apart from that, there is neither a potent antidote nor an effective treatment approach has been yet established for ALPP and supportive care such as correction of metabolic acidosis, hypokalemia and hypoglycemia in addition to monitoring blood pressure and cardiac output is the only choice of treatment which should be executed when necessary by clinical developments (6-10).

In Iran, however, gastric lavage is a standard treatment especially in our center. Although no protocol for gastric lavage has been well defined yet, oral administration of sodium bicarbonate, lavage of potassium permanganate, activated charcoal and vegetable oils are of the recommended first line approaches to ALPP by few authors (3,11,12). This is to decrease the toxin absorption and alkalize blood pH as a compensatory attempt for the inevitable metabolic acidosis (3,11,12).

Nevertheless, many patients die in spite of intensive care and therefore, establishment of new treatment strategy has been always in demand. Thus, in this paper, we demonstrated a novel technique as a primary approach to patients with ALPP due to intentional ingestion of aluminum phosphide tablets. Furthermore, we compared them to patients treated using local classic method of potassium permanganate lavage followed by oral administration of sodium bicarbonate.

Patients and Methods

We conducted this cohort study in Loghman Hakim Poison Hospital (Tehran, Iran) which is a referral center of poisoning in Iran and a center of excellence in Middle East. Between April and November 2009 and after institutional approval for ethics, all cases of ALPP who had intended to commit suicide were considered for the

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study. Amongst them all, patients who: came into the hospital no later than two hours from ingestion, had no vomit after ingestion for one hour, did not solve the pill(s)in water prior to ingestion and had positive silver nitrate test of gastric fluid were enrolled to the study. In contrast, all cases with mixed drug-aluminum phosphide poisoning, chronic toxicity, negative or suspicious silver nitrate test, unknown count of ingested aluminum phosphide tablets and whose time of hospital arrival was longer than two hours (from ingestion time) were excluded.

Then from all patients admitted to the emergency ward for poisoning, total number of 120 patients (67 males, 53 females; mean age 27.4) best fit the inclusion criteria. These patients were allocated into two groups randomly while none of the patients or clinical staff was aware of therapeutic materials in detail. Patients, in whom intubation was necessary, were considered for mechanical ventilation immediately.

First group (control group, Table 1) comprised 60 patients (31 males, 29 females; mean age 26.4) to whom potassium permanganate (1:10000) lavage and oral administration of three vials of sodium bicarbonate (7.5%) via gastric tube were considered (PS). This is actually the classic technique of our center in which, as well as the rest of the world, no efficient antidote is available and charcoal is usually not considered unless for cases of drug overdose regardless of ALPP. The second group (Table 1) comprised other 60 patients (36 males, 24 females; mean age 26.4) who received the new protocol performed as follows: suction of gastric contents using a 50 ml syringe, oral administration of three vials of sodium bicarbonate, potassium permanganate (1:10000) lavage and oral administration of three vials of sodium bicarbonate (SSPS) once again.

Table 1. Age average and number of patients in each of PS and SSPS group for gender.

		patients	**age average**	
		n	***years***	
Male	PS	31	26,06	26
	SSPS	36	25.94	
Female	PS	29	26.72	26.77
	SSPS	24	26.83	

n: number

For each patient the following specifications were recorded: age, sex, number of ingested tablets, presented epigastric pain, nausea, sore throat, heartburn, dyspnea, sense of thirst, necessity of mechanical ventilation on hospital arrival, past history of psychological disorder and past suicidal attempts. In contrast, liver and kidney function tests, pathologic evaluation and autopsy were *not* considered due to the specific design of the study.

When necessary, volume expanders, positive inotropes, pulse oximetry, nasal oxygen therapy were provided.

All gathered data were transferred to SPSS 17 Software and Chi-Square and t-test were used for analysis. Statistical significance level was set as 0.05 or less.

Results

For both SP and SSPS groups, comparison regarding age, sex, indication of intubation, dyspnea, number of ingested pills, presence of epigastric pain, heart burn, sore throat, sense of thirst, nausea, past history of psychological disorders, past history of suicidal attempt(s) and number of attempts with frequency of mortality was performed and results are summarized in table 2.

Table 2. Thirteen factors of which relationship with survival of patients were measures.

	PS		**SSPS**		**PS and SSPS**	
factor	***P*-value**	**mortality risk**	***P*-value**	**mortality risk**	***P*-value**	**mortality risk**
age	-	-	-	-	0.502	n/a
sex	-	-	-	-	0.951	n/a
intubation- ventilation	-	-	-	-	<0.0001	2.06
dyspnea	0.008	1.8	0.709	n/a	-	-
number of pill(s)	-	-	-	-	<0.0001	-
epigastric pain	0.752	n/a	0.141	n/a	0.583	n/a
heart burn	0.592	n/a	0.102	n/a	-	-
sore throat	0.004	-2.35	0.043*	n/a*	-	-
thirst	<0.0001	3.36	<0.0001	4.06	<0.0001	3.64
nausea	0.001	-2.6	0.013	-1.6	-	-
history of psychological disorder(s)	-	-	-	-	0.075	n/a
history of suicidal attempt(s)	-	-	-	--	0.177	n/a
number of suicidal attempt(s)	-	-	-	-	0.482	n/a

*Odds Ratio: 0.063-1.012, Risk Ratio: 0.135-1.141

In addition, frequency of mortality between the two groups was calculated in order to assess the efficacy of the newly proposed gastric lavage approach [suction of gastric contents, oral administration of sodium bicarbonate (three vials), potassium permanganate (1:10000) lavage and oral administration of sodium bicarbonate (again three vials)].

From all 120 patients, 20 cases were intubated and artificially ventilated who all died, however, from the rest of 100 patients, 39 survived and 61 died. This suggests that the risk of mortality in patients who received intubation-ventilation is 2.06 times more than patients without intubation-ventilation (P<0.0001). In parallel, there were significant correlation between dyspnea and classic method of lavage (SP) and patients with dyspnea has more mortality of 1.8 time (P=0.014) in contrast with SSPS group in which no correlation between dyspnea and mortality was found (P=0.765).

Additionally, patients with epigastric pain at hospital arrival time had no more risk of mortality than patients without (P=0.583). Because from 76 patients with epigastric pain, 28 died (36.8%) whereas from other 44 pain-free patients, 20 patients died (45.5%). Moreover, no correlation was found between mortality and each of SP and SSPS (P-value was 0.481 and 0.116, respectively). Similarly, no correlation was found between existence of heart burn and two different treatment strategies (P=0.102 for SSPS and 0.592 for SP). On the contrary, nausea in both groups [SP (p=0.001) and SSPS (P=0.013)] indicates more chance of survival by 2.6 and 1.6 times, respectively.

Furthermore, sore throat had significant correlation with mortality in SSPS (P=0.004) with 1.55 more time risk, however, this correlation did not exist in SP group (P=0.06).

Interestingly, however, mortality risk was 3.64 times more in patients with thirst in comparison to another group (P<0.0001) as 45 out of 58 patients with sense of thirst died (77.5%), however, only 13 out of 62 patients without sense of thirst died (21%). Moreover, in both groups of patients (SP and SSPS), there was a correlation between sense of thirst and mortality rate (P<0.0001) and patients with thirst had more 3.36 and 4.06 times risk of mortality in SP and SSPS groups, respectively.

According to the calculated P-value (0.075), past psychological disorder has no statistical impact on the mortality of patients as 29 out of 66 patients with psychological disorder and 32 out of 53 patients without psychological disorder survived.

Table 3. Number of patients regarding number of ingested pill(s).

ingested pill(s)	patients	patients died
n	*n*	*n (percent)*
1	14	3 (21.5%)
2	35	12 (34%)
3	55	27 (49%)
4	16	16 (100%)
Total	120	58 (43.8%)

n: number

Table 4. Number of dead and recovered patients for gender.

	death	survival	total
	n (percent)	n (percent)	n (percent)
Male	32 (48.5%)	34 (51.5%)	66 (100%)
Femal	26 (48.1%)	28 (51.9%)	54 (100%)
Total	58 (48.3%)	62 (51.7%)	120 (100%)

n: number

Furthermore, neither of prior suicidal history nor number of past suicidal attempts has significant impact on mortality (P=0.177 and 0.482, respectively) and patients with ALPP survive or die regardless of the three mentioned psychological-based parameters. Since from 44 patients with suicidal attempt in their history, 25 cases died (56%) and from 76 patients who had no previous suicidal attempt, 33 cases died (43%). One person (0.8%) had four suicidal attempts; four patients (3.3%) had committed suicide thrice, 13 patients (10.8%) twice and 26 patients (21.7%) once only. However and regarding the number of the ingested pills (Table 3), patients with more ingested tablets had more mortality (P<0.0001).

Above all, comparison between two groups of patients who have been treated differently (PS *versus* SSPS) regarding mortality demonstrated that from 60 patients of SSPS group, 36 recovered and 24 died, however, from 59 patients in SP group, only 25 cases recovered and the rest of 34 died. This suggests the new approach is more efficient in survival of patients, however, the P-value in comparison with the classic gastric lavage method was close to significant level (P=0.054) (Table 4).

Discussion

Aluminum phosphide poisoning (ALPP) is a common poisoning in Asia especially North-Central India, Iran,

Jordan and Morocco (1-5,13). The main cause of this phenomenon is its high utilization in grain storage and transportation facilities which mostly results in accidental poisoning. On the other hand, intentional poisoning for suicide is also common due to its accessibility, inexpensiveness and moreover, its fatal and irreversible effect, as has been reported since especially 80s (14). As no potent antidote has been developed, the only effective approach toward ALPP patients is supportive and critical care to balance blood PH, electrolytes and arterial blood pressure (6-10).

On the contrary and as an Iranian local treatment strategy, oral administration of sodium bicarbonate in addition to potassium permanganate lavage is the currently acceptable first line treatment for ALPP (3,11,15). Additionally, administration of calcium gluconate and magnesium sulfate were considered for most of the patients. According to findings of Shadnia *et al.* there was significant difference between survivors and non-survivors of ALPP regarding blood concentration of bicarbonate (15). This emphasizes the importance of alkalization that is performed as standard approach in this referral center (15). This study is to improve the mentioned treatment strategy to establish a more effective approach through gastric lavage.

First and foremost, we observed that SSPS lavage strategy results in less mortality than classic PS method which is promising, however, this difference was not quite statistically significant (P=0.054).

Apart from that, we showed that the more tablets are ingested, the more mortality will occur. This is as same as Jaiswal *et al*. paper in which number of ingested tablets have been considered as the most important prognostic factor in survival of ALPP patients (7). Whereas, Singh *et al*. emphasized that dose of ingested drugs has no impact on prognosis of patients in contrast with number of vomits (16).

From respiratory failure standpoint, our study proposed worse prognosis in patients with respiratory aid on time of hospital arrival as all of intubated-ventilated patient died. Although this may first bring the negative impact of intubation-ventilation on prognosis, it should be borne in mind that this group of patients is of the poor general condition and death was inevitable in case no supportive care is regarded. Moreover, patients with dyspnea in SP had more risk of mortality while Jaiswal and colleagues reported only one patient with gasping who needed intubation among their 40 ALPP patients (7).

Gastrointestinal manifestations recorded in our study were epigastric pain, heartburn and nausea. According to our findings, neither epigastric pain nor heartburn has impact on patients' survival, whereas, patients with nausea had more survival chance for 1.6 and 2.6 more times in SSPS and SP groups respectively. Additionally, sense of thirst represents more risk of mortality in both groups (4.06 times in SSPS and 3.36 times in SP). We postulate that sense of thirst and nausea are symptoms of metabolic imbalance that occur in patients of worse general condition, however, epigastric pain and heartburn may relate to the personal sensitivity of gastric tissue to drugs.

In addition, sore throat can be considered as a prognostic factor in whom SSPS was applied and represents 1.5 less chance of survival.

According to our findings, 4-step-gastric lavage [suction of gastric contents using a 50 ml syringe, oral administration of three vials of sodium bicarbonate (7.5%), potassium permanganate (1:10000) lavage and again oral administration of three vials of sodium bicarbonate (SSPS)] is a more effective washing method than what has being used for many years in our center [potassium permanganate (1:10000) lavage and oral administration of three vials of sodium bicarbonate via gastric tube (PS)]. Moreover, indication of intubation-ventilation, sense of thirst, sore throat and absence of nausea can be considered as reliable prognostic factors in survival of all ALPP patients.

Nevertheless and according to insignificant different between the two method, more thorough studies should be conducted to assess its therapeutic efficacy. In conclusion, we demonstrated the efficacy of our new gastric lavage method (SSPS) over SP method which did not show statistical difference. In addition, indication for intubation-ventilation, sense of thirst, sore throat and absence of nausea are hypothesized to be reliable prognostic factors.

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